

REMARKS

I. Explanation of Amendments to the Specification

The foregoing amendment is in the revised amendment format as provided in 1267 OG 106 (25 February 2003). Accordingly, the provisions of 37 C.F.R. § 1.21, requiring submission of clean and marked-up versions of the replacement paragraphs, are waived. The amendments to the specification are consistent with amendments filed in related applications (see *e.g.*, U.S. Patent Nos. 6,440,698 and 6,420,534) and are directed to typographical errors and other housekeeping matters as explained below.

The application describes two human forms of the Asp2 protease (“Asp2(a)” and “Asp2(b)” splice variants) which differ from each other by the presence or absence of an internal stretch of about twenty-five amino acids. The Applicants believe that they have remained consistent and accurate in their presentation of the sequences for these splice variants, *e.g.* in Figures 2 and 3, but have identified inconsistencies in their applications relating to the names that are the subject of amendments set forth above.

More particularly, the present application refers to the longer splice variant as “Asp2(a)” and the shorter splice variant as “Asp2(b).” However, the Applicants have identified a few instances in the present application of inconsistencies, *i.e.*, where “Asp2(a)” is used to refer to the shorter splice variant and “Asp2(b)” to the longer. The present amendment eliminates the inconsistencies.

The Brief Description of Figures 2 and 3 contained one such inconsistency, and the amendments at pages 23 and 24 correct it. Figure 2 plainly depicts the “shorter” Asp2 sequence, and its description has been amended to recite “Asp2(b)” and to cross reference the shorter sequences in the Sequence Listing. The opposite amendment has been made for Figure 3, which plainly depicts the “longer” Asp2 sequence.¹ A similar amendment is made at page 49, where the application contains cross-references to Figures 2 and 3. The foregoing amendments ensure that the Specification consistently refers to the “longer” Asp2(a) polynucleotide and polypeptide as having the sequences set forth in SEQ ID NOS: 3 and 4, and the “shorter” Asp2(b) as having the sequences set forth in SEQ ID NOS: 5 and 6.

¹ In the description of Figure 3, the sentence pertaining to denoting the transmembrane domain has been deleted because the Figure lacks brackets and because the transmembrane domain is identified elsewhere in the specification.

These amendments are supported by the application as filed because they simply make the terminology more consistent, and the inconsistencies and the manner in which they should be corrected would have been apparent to any reader of ordinary skill in the art.

The amendment at page 12 of the application addresses an informality identified by the Examiner in a related application and does not introduce new matter or change the meaning of the application in any way.

The amendments at pages 32 and 33 correct obvious typographical errors. The domains of SEQ ID NO: 6, as recited at amended pages 32 and 33, are described elsewhere in the specification. See page 21, lines 11-17 and page 50, lines 1-9. It is apparent from the context of the application at pages 32-33 that the Applicants are describing various fragments of Asp2 long and short forms and that some of the references to portions of the short form inadvertently refer to SEQ ID NO: 4 instead of SEQ ID NO: 6. For example, it is apparent to a reader that the six paragraphs spanning page 31, line 27, to page 32, line 15, are essentially identical to the six paragraphs spanning page 32, line 16, to page 33, line 5, except that the former refer to portions of SEQ ID NO: 4 and the latter are supposed to refer to corresponding portions of SEQ ID NO: 6, which has an internal deletion of 25 amino acids relative to SEQ ID NO: 4. Although the first three references correctly specify SEQ ID NO: 6, the others require correction to refer to SEQ ID NO: 6. The error is especially evident at page 32, lines 21-22, which explicitly refer back to two preceding paragraphs that recite SEQ ID NO: 6, making clear that another reference to SEQ ID NO: 6 was intended. Therefore these amendments do not add new matter to the specification.

II. Restriction

Citing 35 U.S.C. § 121, the Examiner alleged that claims 1-150 were drawn to fourteen distinct inventions:

1. Claims 1-23 and 139-140, drawn to a method for producing a polypeptide comprising SEQ ID NO: 63 comprising polynucleotide, vectors, and host cells comprising same.

2. Claims 26-28, 29-35 and 142 (each in part), drawn to a method for producing a polypeptide comprising SEQ ID NO: 7 comprising polynucleotide, vectors, and host cells comprising same, and the polypeptide comprising SEQ ID NO: 7.

3. Claims 24-25, 38-46, and 141-142 (each in part), drawn to a method for producing a polypeptide comprising SEQ ID NO: 8 comprising polynucleotide, vectors, and host cells comprising same, and the polypeptide comprising SEQ ID NO: 8.

4. Claims 47-54, 58-60, 62-70, and 142 (each in part), drawn to a method for producing a polypeptide comprising SEQ ID NO: 4 comprising polynucleotide, vectors, and host cells comprising same, and the polypeptide comprising SEQ ID NO: 4.

5. Claims 47-48, 55-57, 61-64, 71-82, and 142 (each in part), drawn to a method for producing a polypeptide comprising SEQ ID NO: 6 comprising polynucleotide, vectors, and host cells comprising same, and the polypeptide comprising SEQ ID NO: 6.

6. Claims 83-87, 89-95, 143, and 147, drawn to a method for assaying for modulators of β -secretase activity wherein the substrate polypeptide of the second composition comprises SEQ ID NO: 63.

7. Claims 83-86, 88-95, and 143, drawn to a method for assaying for modulators of β -secretase activity wherein the substrate polypeptide of the second composition comprises SEQ ID NO: 67.

8. Claims 96 and 97, drawn to a method of identifying agents that inhibit the activity of human Asp2 aspartyl protease (Hu-Asp2).

9. Claims 98-102, drawn to a method involving nucleotide sequences.

10. Claims 103, 107, 120, and 123 drawn to a method for treating Alzheimer's disease.

11. Claims 104-106, 108-119, 124-129, 144-146, and 148-150 drawn to a method for identifying agents that inhibit the activity of human Asp2 aspartyl protease (Hu-Asp2).

12. Claims 121-122, drawn to a method for identifying agents that modulate the activity of human Asp2 aspartyl protease (Hu-Asp2).

13. Claims 130-137, drawn to a method of reducing cellular production of amyloid beta from amyloid precursor protein using an anti-sense reagent.

14. Claim 138, drawn to a method of diagnosing Alzheimer's disease.

III. Election

The Applicants hereby elect Group 4, which includes claims 47-54, 58-60, 62-70 and 142 drawn in part drawn to a method for producing a polypeptide comprising SEQ ID NO: 4 comprising polynucleotides, vectors, and host cells comprising same, and the polypeptide comprising SEQ ID NO: 4.

IV. Traversal of Restrictions

A. Applicants traverse the restriction of Groups 4 and 9 and/or 11.

The methods of Groups 9 and 11 identify an agent that inhibits the activity of human Asp2 aspartyl protease by contacting a hu-Asp2 polypeptide, such as a polypeptide of Group 4, and APP in the presence and absence of a test agent. If the polypeptides of Group 4 (product claims) are found novel and non-obvious under 35 U.S.C. §103(a), the Applicants may be entitled to rejoinder of claims to methods of using that product. *See* 1184 OG 86, (1996). The Applicants hereby request that, if the product claims of Group 4 are allowed, the Patent Office rejoin the method claims of Groups 9 and 11. To facilitate efficient examination, the Applicants request that the claims of Groups 4, 9 and 11 be examined simultaneously. The relatedness of the claims of Groups 9 and 11 to the claims of Group 4 suggest that there will be no serious burden involved. Applicants respectfully request that the restriction requirement, in respect to Groups 4, 9 and 11 be withdrawn and these groups be examined simultaneously.

B. Applicants traverse the restriction of Groups 4 and 12.

The Group 12 methods of identifying an agent that modulates the activity of human Asp2 aspartyl protease by contacting an Asp2 aspartyl protease, such as a polypeptide of Group 4, and APP in the presence and absence of a test agent. If the polypeptides of Group 4 (product claims) are found novel and non-obvious under 35 U.S.C. §103(a), the Applicants may be entitled to rejoinder of claims to methods of using that product. *See* 1184 OG 86, (1996). The Applicants hereby request that, if the product claims of Group 4 are allowed, the Patent Office rejoin the method claims of Groups 12. To facilitate efficient

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examination, the Applicants request that the claims of Groups 4 and 12 be examined simultaneously. The relatedness of the claims of Groups 12 to the claims of Group 4 suggest that there will be no serious burden involved. Applicants respectfully request that the restriction requirement, in respect to Groups 4 and 12 be withdrawn and these groups be examined simultaneously.

CONCLUSION

In light of the forgoing remarks, the Applicants request withdrawal of the restriction requirement in light of Groups 4, 9, 11 and 12.

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Respectfully submitted,

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